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Impact of ambient temperature on clinical visits for cardio-respiratory diseases in rural villages in northwest China

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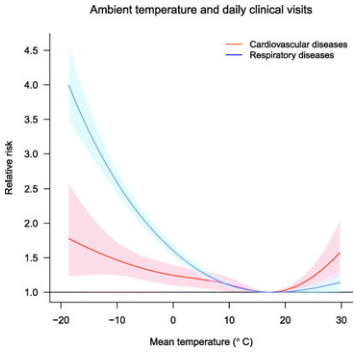
HIGHLIGHTS

- Temperature and cardio-respiratory clinical visits was studied in rural China.
- An U-/reverse J-shaped association was found for the two illness, respectively.
- Extreme cold was stronger and immediate on respiratory disease.
- Moderate cold resulted in most of the temperature-related clinical visits.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: The association between temperature and cardio-respiratory disease in urban areas has been widely reported but there is limited information from populations living in rural areas that may be disproportionately affected by climate change.
Objectives: To quantify the associations between daily temperature and clinical visits due to cardiovascular and/or respiratory disease in rural villages in the Ningxia Hui Autonomous Region, China over 2012–2015.
Methods: Daily data on clinical visits and weather conditions were collated from 203 villages. A quasi-Poisson regression with distributed lag non-linear model was used to examine the associations between daily temperature and clinical visits up to 28 days, after controlling for potential confounders.
Results: Over three years, 158,733 and 1,272,212 clinical visits were recorded for cardiovascular and respiratory diseases, respectively. Both low and high temperatures were associated with an increased risk of clinical visits for cardiovascular-related conditions, whereas only low temperatures were associated with increased clinical visits related to respiratory illness. The cold effect on cardiovascular visits appeared at the lag 6th day and persisted until the 22nd day, resulting in a cumulative relative risk (RR) 1.55 (95% CI: 1.26–1.92), compared with the minimum-clinical visit temperature. The cold effect on respiratory visits appeared immediately and lasted over the lag 0–28 days, with a cumulative RR 2.96 (2.74–3.21). Suboptimal temperature accounted for approximately 13% and 26% of clinic visits due to cardiovascular and respiratory disorders, respectively, with the majority of cases attributable to moderate – rather than extreme – cold temperature.

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Conclusions: In rural settings, sub-optimal temperatures explained nearly one quarter of all clinical visits due to cardiovascular and respiratory diseases. Although extreme cold temperature had a stronger, more immediate, prolonged effect on respiratory disease than for cardiovascular disease, moderately cold temperatures accounted for most of the overall burden of clinical visits.

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1. Introduction

Worldwide, the last 30 years has been the warmest period since 1880, accompanied by more extreme hot temperature events while cold extremes remain (Guha-Sapir et al., 2017; Morak et al., 2013; NOAA National Centers for Environmental information, 2017). There is sound evidence indicating that both extreme cold and hot temperatures induce substantial physiological stress on the human body and both temperature extremes are associated with a range of health outcomes resulting in increased morbidity and mortality (Gasparrini et al., 2015; Zhang et al., 2017). Globally, cardiovascular and respiratory diseases, which have been demonstrated to be strongly associated with both cold and hot temperatures (Basu, 2009; Mäkinen et al., 2009; Michelozzi et al., 2009), are among the leading causes of mortality resulting in >26 million deaths each year, with >75% of cases occurring in low- or middle-income countries (World health Organization, 2017).

Previous studies in China have mainly focused on the associations between temperature and all-cause or cause-specific mortality with little consideration of the potential effect on morbidity (Guo et al., 2012b). For example, although cardio-respiratory diseases account for approximately 30% of annual hospital admissions and health-care costs (National Health and Family Planning Commission of the PRC, 2016), there is limited information regarding the possible impact of suboptimal temperature on these outcomes (Guo et al., 2012a; Wang et al., 2013). Importantly, few studies in China have directly compared the association between temperature with cardiovascular and respiratory diseases within the same study population, which is necessary to fully understand how temperature variation impacts on these health outcomes at the population level (Liu et al., 2011).

In China, evidence regarding the health burden associated with suboptimal temperatures has been derived chiefly from large cities (Li et al., 2014; Tian et al., 2012), with limited information from rural areas where the incidence of cardiovascular and respiratory disease is the highest (National Health and Family Planning Commission of the PRC, 2016). The Ningxia Hui Autonomous Region, one of the most undeveloped regions in China, comprises the Loess Plateau, Mongolian Plateau and Tibet Plateau, and is an area with wide variation ranges of monthly temperature (25.2–31.2 °C) and diurnal temperature (12–15 °C) (Bureau of Statistics of Ningxia Hui Autonomous Region, 2016; China Weather Network, 2010). The average temperature in this region has increased by 1.5 °C since the 1960s, accompanied by abnormal temperature events, such as dry-hot winds and cold spells, occurring frequently all year round (China Weather Network, 2010). Such events may increase the incidence of cardiovascular and respiratory disease in the population. Moreover, any effects could be exacerbated by the regions' poor infrastructure and limited health resources, especially for residents in the poorest counties of Haiyuan and Yanchi (National Bureau of statistics of the People's Republic of China, 2015b).

The aim of this study was to quantify the associations between daily temperature and clinical visits for cardiovascular and respiratory diseases in rural villages in the Ningxia Hui Autonomous Region of China during 2012–2015. Evidence generated by this study could be used to guide policy makers with respect to the allocation of health resources and the development and implementation of adaptive strategies in regions at greatest risk of extreme temperature perturbations.

2. Material and methods

2.1. Data collection

Between 1 January 2012 and 31 December 2015 daily data on clinical visits associated with cardiovascular and respiratory illness were collected from medical centres located in villages of the Haiyuan and Yanchi counties, Ningxia Hui Autonomous Region. Local patients were diagnosed and recorded by village physicians. Considering the possible misclassification in the primary medical centres in China, especially in the rural areas, we did not analyse the association between temperature and subtypes of cardiovascular and respiratory diseases. By 2015, there were 165 villages under 17 towns or townships in Haiyuan county, and 102 villages under 8 towns or townships in Yanchi county (National Bureau of statistics of the People's Republic of China, 2015a). Our data collection indicated that in some villages there were substantial missing records in certain dates. In this study villages with <180 days records in a specific year were treated as of poor quality and excluded from further analysis. Considering core living areas of towns or townships usually far from other villages, data from these areas were included in this study which were defined as separate villages. In total, data were available from 134 and 69 villages from the two counties, respectively (Fig. 1). Village-specific population data were collected from the 2010 Census published by the National Bureau of statistics of the People's Republic of China (http://www.stats.gov.cn).

Daily data on meteorological conditions during the study period were collected from 839 city- or county-based meteorological stations across China, including daily mean temperature, relative humidity, wind speed, and sunshine hours, through China Meteorological Data Sharing Service. Village-specific meteorological variables were obtained using different approaches. Specifically, daily mean ambient temperature and relative humidity in the centroid of each village were interpolated from the data of the 839 stations using ordinary kriging model as described by Guo et al. (2013). Daily data on wind speed and sunshine hours in each village were replaced by the records from nearest meteorological stations.

2.2. Data analysis

A quasi-Poisson regression with distributed lag non-linear model (DLNM) was applied, using time series designed data from each village, to examine the associations between mean daily temperature and clinical visits for cardiovascular and respiratory diseases, respectively. The generalised additive mix model was used to perform quasi-Poisson regression to control for the random effect of each village. In addition, the models controlled for the following parameters: long-term trend, seasonality, day of the week, public holidays, and village-specific population sizes. The full model is described as follows:

$$Y_{it} \sim Poisson\ (\mu_{it})$$

$$Log\ \ (\mu_{it}) = \alpha + \beta Tem_{it} + \gamma Strata_{it} + \delta DOW_{it,} + \varepsilon Holiday_{it} + \text{offset}\ (LOGPOP_i) + \pi Z_i$$

where Y_{it} represents the daily counts of cardiovascular or respiratory visits at village i on day t; α is the intercept; Tem_{it} is the cross-basis matrix for modeling the temperature effect over lag 0–28 days (Bhaskaran et al., 2010; Guo et al., 2011); $Strata_{it}$ is a categorical variable of year and calendar month to control for the long-term trend and seasonality; DOW_{it} is a categorical variable to control for the effect

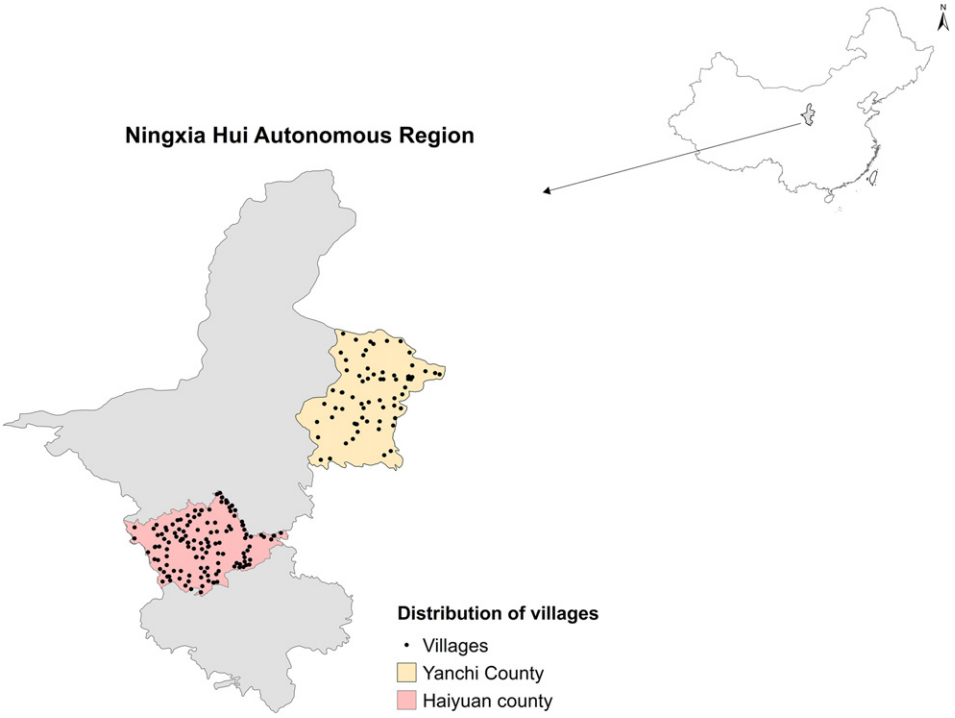

Fig. 1. Distribution of 203 villages in Haiyuan and Yanchi counties in Ningxia Hui Autonomous Region, China.

of day of the week; $Holiday_{it}$ is a binary variable, the value of which is 1 if day t is public holiday while 0 if not; $LOGPOP_i$ is the population size in village i on the log scale; Z_i is a random intercept for villages; and β, γ, δ, ε and π are the coefficients of corresponding terms.

The initial analysis indicated that a natural cubic spline with 4 degrees of freedom (dfs) for temperature and 3 dfs for lag produced the best model fit, which was subsequently applied to the data. Relative risks (RRs) and 95% confidence intervals (CI) for cardiovascular and respiratory visits associated with respective temperature values were calculated by setting the reference at the temperature with the lowest risk of clinical visits (MVT). Extreme cold and hot effects were defined as RRs at the 1st and 99th percentiles of the temperature range, compared with MVT. Absolute number and percentage of cardiovascular and respiratory visits attributable to overall suboptimal temperature, moderate cold and heat, and extreme cold and heat during the study period were calculated, with empirical CIs estimated by Monte Carlo simulation (5000 random samples), using the approach described by Gasparrini and Leone (2014). The overall suboptimal temperature was defined as the temperature range except MVT. The moderate cold and heat were defined as the ranges between MVT with 1st percentile and 99th percentile of temperatures. The extreme cold and heat were temperatures at 1st percentile of temperature or below, and at 99th percentile of temperature and above, respectively.

Sensitivity analyses were performed by changing the maximum lag from 28 to 31 days to explore whether lag 0–28 days could fully capture the exposure-lag-response associations. Other meteorological variables including relative humidity, wind speed and sunshine hours were also introduced into the model stepwise to examine their potential modification effects on the association between temperature and clinical visits using the same DLNM as temperature itself.

Some air pollutants are also associated with cardiovascular and respiratory diseases (Hoek et al., 2013), but we were unable to assess any potential effect modification due to lack of data on pollution for the study area. However, our multi-city study has shown the modification effects of air pollutants (including $PM_{2.5}$, SO_2, CO and NO_2) are negligible on the association between temperature and morbidity in urban areas of China (Zhao et al., 2017). This means the temperature-morbidity association was robust whether we control for outdoor air pollutants or not. Because the quality of outdoor air is much better in rural areas than in cities (Zhou et al., 2014), we believe the present study gives unbiased effect estimates.

All data analyses were performed using R software (version 3.3.2). The "dlnm" package was used to fit DLNM (Gasparrini, 2011; Gasparrini et al., 2010).

3. Results

Table 1 shows the summary statistics for the number of clinical visits for cardiovascular and respiratory diseases from 203 villages from 1 Januaray 2012 to 31 December 2015. In total, there were 158,733 clinical visits for cardiovascular diseases and 1,272,212 visits for respiratory diseases with a daily average of 109 and 871 cases, respectively, during this time period. The average temperature in the 203 villages was 8.5 °C (−18.6 to 29.7 °C).

The association between temperature and daily cardiovascular visits was U-shaped, with greatest risk occurring at both low and high

Table 1
Summary of daily clinical visits for cardiovascular and respiratory diseases in the 203 villages in Ningxia Hui Autonomous Region, China between 1 January 2012 and 31 December 2015.

	Total cases		Daily cases [mean (range)]	
	Cardiovascular visits	Respiratory visits	Cardiovascular visits	Respiratory visits
Gender				
Male	75,472	717,892	52 (5, 117)	491 (111, 1 2467)
Female	83,261	554,320	57 (2, 134)	379 (66, 1069)
Age (years)				
0–5	937	129,599	2 (1, 8)	89 (15, 250)
6–14	715	183,213	1 (1, 4)	125 (14, 522)
15–34	13,001	381,400	9 (1, 28)	261 (38, 834)
35–64	87,167	469,545	60 (5, 136)	321 (69, 817)
65+	56,913	108,455	39 (1, 91)	74 (9, 172)
Total	158,733	1,272,212	109 (9, 224)	871 (180, 2536)

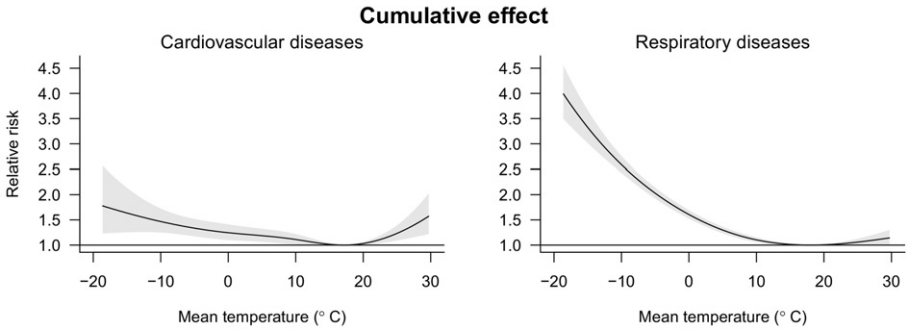

Fig. 2. Cumulative associations between temperature and daily clinical visits for cardiovascular diseases and respiratory diseases over lag 0–28 days. Natural cubic spline with 4 degrees of freedom (dfs) was used for temperature and 3 dfs for lag, respectively.

temperatures and the nadir at 17.3 °C (Fig. 2). As shown in Table 2, the RR for 28-day cumulative effect of extreme cold temperature (1st percentile of temperature) on daily cardiovascular visits was 1.55 (95% CI: 1.26–1.92), while the RR for extreme heat (99th percentile of temperature) was 1.28 (1.11–1.48). In comparison, a reverse J-shaped relation between daily temperature and respiratory visits was observed, that is, the risk of daily respiratory visits only increased during cold days, with RR at 2.96 (95% CI: 2.74–3.21) compared with the MVT.

Fig. 3 shows the lag effects of extreme cold and hot temperatures on clinical visits for cardiovascular and respiratory diseases. The effect of extreme cold on daily cardiovascular and respiratory visits produced different lag patterns. The effect of extreme cold on frequency of clinical visits due to cardiovascular disease appeared at the 6th lag day, peaked at the 14th day and then declined after the 22nd day. In comparison, the effect of extreme cold on clinical visits due to respiratory illness was immediately apparent and peaked at the 9th day and thereafter, gradually declined. The effect of extreme heat on frequency of clinical visits due to cardiovascular disease was apparent at day 6 and persisted until day 25.

Table 3 shows both the proportion, and the absolute number of clinical visits due to cardiovascular and respiratory disease, that could be attributable to different non-optimum temperature components. Overall, 24.5% of clinical visits (350424), including 13.1% (95% empirical CI: 7.2–18.3%) of cardiovascular visits (20759) and 25.9% (32.5–28.0%) of respiratory visits (329665), could be explained by suboptimal temperatures. Cold temperatures were responsible for 11.5% (5.6–16.7%) of visits due to cardiovascular disease and 27.7% (23.5–27.8%) of respiratory visits, respectively. In comparison, the number of clinical visits attributable to high temperatures was smaller: 1.6% (0.6–2.5%) for cardiovascular disease and 0.2% (−0.1 to 0.5%) for respiratory disease.

Most of the attributable burden for clinical visits due to suboptimal temperatures could be explained by moderate, rather than extreme, temperature perturbations: moderate deviations in temperature explained 12.5% of cardiovascular visits (19881) and 25.2% of respiratory visits (320644), whereas extreme temperatures explained approximately 0.7% of all clinical visits due to cardiovascular (0.6%) and respiratory (0.7%) diseases.

Sensitivity analyses showed that the main results did not materially change when altering the maximum lag from 28 to 31 days (see Supplementary Fig. 1). The results were robust when adding other meteorological variables to the models (see Supplementary Fig. 2).

4. Discussion

This is the first study to examine the nature of the associations between daily temperature and risk of clinical visits, due to two major health outcomes in a large rural population in northwest China. The relationship between temperature and clinical visits due to cardiovascular and respiratory disease differed: for cardiovascular outcomes the association was U-shaped, whereas, there was a reverse J-shaped relation for clinical visits due to respiratory disease. Although the risk of clinical visits was substantially higher during periods of extreme cold or heat, most of the clinical visits attributable to fluctuations in temperature were caused by moderate deviations in temperature. Moreover, cooler, rather than warmer, temperatures, accounted for a greater proportion of the number of clinical visits, a finding consistent with earlier studies (Gasparrini et al., 2015). Overall, one quarter of clinical visits due to cardiovascular and respiratory outcomes in the 203 villages could be explained by exposure to suboptimal temperature, with the temperature-related fraction due to respiratory illness twice that due to cardiovascular disease.

Extreme cold had a weaker, delayed and short-lived effect on the risk of cardiovascular visits, but a stronger, immediate and more sustained effect on clinical visits due to respiratory illness. In contrast, extreme heat was not strongly associated with the risk of clinical visits for respiratory visits. A possible explanation for the differential effect of temperature, is that compared with the cardiovascular system, the respiratory tract is more directly exposed to external air rendering it more susceptible to air-borne contagions (Tortora and Derrickson, 2008). For example, exposure to a cold environment has been shown to increase the risk of respiratory tract infections such as acute laryngitis as well as exacerbation of chronic obstructive pulmonary disease (Donaldson et al., 1999; Mäkinen et al., 2009).

To the best of our knowledge, this is one of the first studies to demonstrate that exposure to moderately low temperatures is associated with an increased risk of clinical visits due to respiratory disease in a rural setting in China. Other studies from large urban areas of China or other countries have reported a positive correlation between heat and hospitalisations for respiratory disease (Ma et al., 2011; Turner et al., 2012), highlighting the importance of examining urban and rural settings separately. Aside from differences in rurality, direct comparison between studies is hampered by differences in the definitions that have been used to indicate extreme cold and heat. In the study by Ma

Table 2
Relative risk (95% confidence intervals) for clinical visits attributable to cardiovascular disease and respiratory disease associated with extreme cold (1st percentile) and heat (99th percentile) over lag 0–28 days.

Diseases	Extreme cold (95% CI)	Extreme heat (95% CI)	Minimum-visit temperature (°C)
Cardiovascular visits	1.55 (1.26, 1.92)	1.28 (1.11, 1.48)	17.3
Respiratory visits	2.96 (2.74, 3.21)	1.07 (0.99, 1.15)	18.0

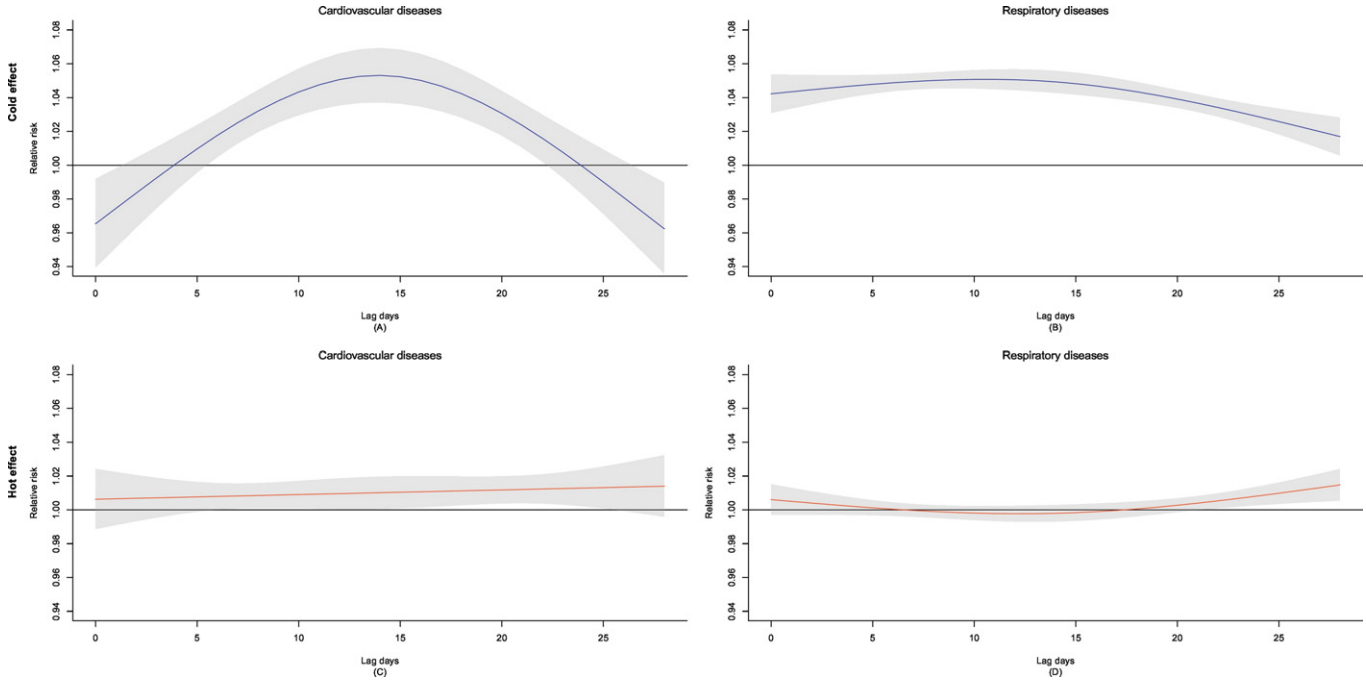

Fig. 3. Lagged effect of extreme cold (1st percentile) and heat (99th percentile) on daily clinical visits for cardiovascular diseases and respiratory diseases over 0–28 days. Natural cubic spline with 4 degrees of freedom (dfs) was used for temperature and 3 dfs for lag, respectively.

and colleagues, the definition of extreme heat was >35 °C while in our study, the definition was roughly 26 °C, which is significantly closer to a comfortable living temperature (Hansen and HE Burroughs, 2013; Meng, 1990). Our findings that clinical visits, due to cardiovascular disease, are sensitive to both low and high temperatures is in agreement with findings from previous studies derived from both urban and rural areas (Brunetti et al., 2014; Phung et al., 2016; Urban et al., 2014; Yu et al., 2011). Several factors may explain the high risk of cardiovascular diseases during cold days, such as physiological increase of blood pressure/heart rate after exposing to low temperature and rising plasma triglyceride due to overtake of calories in winter (Hokanson and Austin, 1996; Madaniyazi et al., 2016). Fasting plasma glucose, which is higher during cold seasons, is also associated with cardiovascular diseases, especially for patients with diabetes mellitus (Barr et al., 2007; Held et al., 2007; Li et al., 2016). Extreme heat, on the other hand, may also induce anomaly of heart rate and stress the circulatory system (high blood viscosity and hypotension) (Keatinge et al., 1986; Kim et al., 2012; Ren et al., 2011).

Previous research has focused on the health risks associated with extreme temperature events such as cold spells and heatwaves, with limited information regarding the health effects of more moderate deviations in temperature from the MVT, which is a more frequent occurrence (Anderson and Bell, 2009; Huynen et al., 2001). In this study, we observed that exposure to moderate temperature, especially to mildly cold temperatures, explained most of the temperature-related clinical visits. Specifically, the attributable fraction of clinical visits due to respiratory illness was higher than that due to cardiovascular visits. In contrast, only a very small fraction of the total number of clinical visits during the three year period was explained by extreme heat.

In China, rural areas usually experience cooler temperatures than cities, due to less anthropogenic activities and heat sources, lower density of high buildings, and more green spaces (Liu et al., 2009; National Bureau of statistics of the People's Republic of China, 2015b). In periods of hot weather, this may be particularly beneficial to rural compared with urban residents, as suggested by previous studies comparing the urban-rural differences of temperature-related health burdens (Gabriel and Endlicher, 2011; Hajat et al., 2007; Urban et al., 2014). However, overall, the lower temperatures experienced in rural compared with urban areas may be a contributing factor to the burden of cardio-respiratory diseases, especially when considering that most temperature-related clinical visits could be attributed to moderately cold temperatures as opposed to extreme cold.

Table 3
Fraction (%) and absolute number of cardiovascular and respiratory visits attributable to overall suboptimal temperature, moderate cold and heat, and extreme cold and heat in the 203 villages between 1 January 2012 and 31 December 2015.

	Attributable cardiovascular visits (95% empirical CI)		Attributable respiratory visits (95% empirical CI)		Total visits
	Fraction (%)	Total visits	Fraction (%)	Total visits	
Overall	13.08 (7.15, 18.31)	20,759 (11,353, 29,062)	25.91 (23.46, 27.96)	329,665 (298,495, 355,748)	350,424
Cold	11.50 (5.61, 16.65)	18,260 (8903, 26,428)	25.72 (23.50, 27.76)	327,276 (298,936, 353,108)	345,536
Extreme cold	0.24 (0.12, 0.33)	383 (191, 526)	0.69 (0.66, 0.72)	8786 (8389, 9137)	9169
Moderate cold	11.26 (5.32, 16.44)	17,877 (8441, 26,091)	25.03 (22.74, 27.27)	318,489 (289,356, 346,930)	320,493
Heat	1.57 (0.55, 2.49)	2499 (875, 3959)	0.19 (−0.10, 0.45)	2389 (−1306, 5725)	4888
Extreme heat	0.31 (0.15, 0.45)	496 (233, 717)	0.02 (0.00, 0.04)	234 (7, 457)	730
Moderate heat	1.26 (0.41, 2.06)	2004 (652, 3264)	0.17 (−0.06, 0.40)	2155 (−725, 5027)	4158

The overall suboptimal temperature is defined as the temperature range except the temperature associated with the minimum number of clinical visits (MVT);
The moderate cold and heat are temperature ranges between MVT with 1st percentile and 99th percentile of temperatures;
The extreme cold and heat are temperature ranges at 1st percentile of temperature or below, and at 99th percentile of temperature and above, respectively;
Empirical confidence intervals (CI) were calculated using Monte Carlo simulation (5000 random samples).

In coming decades, the mean temperature in rural areas is expected to increase due to global warming and stepped-up urbanization (Hartmann et al., 2013; Watts et al., 2015). If so, then given the associations between temperature and clinical visits observed in the current study, small increments in temperature may result in a reduced burden of clinical visits due to cardiovascular and respiratory illness in rural regions of China (although, an opposing effect would be expected for more urbanised areas).

There are several limitations of this study. First, meteorological data were site-based and the lack of individual measurements may have introduced potential measurement error. However, this randomly distributed bias is likely to have underestimated the exposure-response association among the population (Guo et al., 2013). Second, indoor air pollution derived from combustion of wood and other fuels during cooking may be a more serious hazard for rural women (Baumgartner et al., 2011). As other time series studies, we were unable to control its potential modification effect of indoor air pollution due to the difficulty of individual measurements. Therefore, the potential for residual confounding by indoor air pollutants remains. Second, we did not analyse the association between temperature and major subtypes of cardiovascular (*e.g.* ischemic and haemorrhagic stroke) and respiratory disease, in order to avoid introducing bias due to misclassification of outcome. This was an *a priori* decision due to the fact that information on health outcomes were obtained from primary medical centres in rural China which are often not equipped to permit reliable diagnosis of disease subtypes. We also did not perform subgroup analyses based on age or gender due to small numbers in some of the analytical cells. Third, this study focused only on two national-level poor counties in northwest China, which limits the generalisability of our findings. Previous studies have indicated that the health impact of suboptimal temperature varies by latitudes, which remains to be determined by future studies (Ma et al., 2015; Zhao et al., 2017).

5. Conclusions

This is the first study simultaneously exploring the association between ambient temperature and clinical visits for cardio-respiratory diseases in rural China. We observed a U-shaped association between temperature and cardiovascular visits and a reverse J-shaped association for respiratory visits, respectively. Extreme cold had an immediate, more prolonged and stronger effect on clinical visits due to respiratory disease than for cardiovascular outcomes. Non-optimal temperature – in particular, moderately cold temperatures - could explain a substantial proportion of all clinical visits due to these two important health outcomes. Future studies are warranted to further quantify the likely effect of climate change on health-service utilisation in rural and urban areas separately.

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Potential conflicts of interest

None declared. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.scitotenv.2017.08.244.

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